rable to mepolizumab 250mg. Active treatments were comparable regarding asthma exacerbations and discontinuations due to AE.

PRS7

COMPARATIVE EFFECTIVENESS ANALYSIS OF MAB IN ASTHMA: THE IMPORTANCE OF EXACERBATION DEFINITION

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OBJECTIVES: Several monoclonal antibodies (mAb) are in development for the treatment of uncontrolled asthma. Network meta-analysis (NMA) will become unavoidable to compare effectiveness of these products. It could only be performed if studies define outcomes similarly. The objective of this research is to review the consistency of exacerbation definition used in clinical trials of mAb. **METHODS:** All mAbs approved or in phase II/III development in asthma were identified through a systematic review in Medtrack® database. Clinical trials were identified through the clinical.trials.gov registry. Exacerbation definition was searched for all identified trials through targeted literature search. Definitions were compared to the current European Respiratory Society, American Thoracic Society and Global Initiative for Asthma guidelines. **RESULTS:** Sixteen mAbs were identified in phase II/III development for asthma. Omalizumab is the only mAb approved for asthma and its pivotal trials occurred over 10 years ago. 95 clinical trials have been registered for these mAbs with 52 trials using exacerbation as a clinical endpoint. Exacerbation definitions were retrieved for 25 trials, among which 40% of trials defined clinical or clinically relevant exacerbation, 12% defined severe exacerbations and 48% defined exacerbation without specification of severity or clinical relevance. Definitions used in trials were not aligned with current guideline definitions, and were inconsistent between studies. Criteria used to define exacerbation included: rescue systemic corticosteroid, use of nebulization therapy, hospital or emergency room admission, unscheduled medical intervention, unscheduled outpatient visits, increased daily dose of rescue inhalers, worsening of symptoms, peak expiratory flow or FEV1 deterioration. **CONCLUSIONS:** High variability of outcome definitions suggests future hurdles for mAb to generate comparative effectiveness through NMA. Head-to-head comparison of the products reaching market in the next years is not expected, and health technology assessment around the extent of additional benefit might be challenging.

PRS8

BAYESIAN NETWORK META-ANALYSIS TO ASSESS THE COMPARATIVE EFFICACY AND SAFETY OF TREATMENTS FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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OBJECTIVES: To assess the comparative efficacy and safety of inhaled corticosteroids and long-acting beta-agonist (ICS/LABA) fixed doses combination and phosphodiesterase-4 inhibitor for chronic obstructive pulmonary disease (COPD), using a Bayesian network meta-analysis. **METHODS:** A systematic literature review was conducted according to NICE guidelines. Outcomes of interest included through forced expiratory volume in one second (FEV1), COPD exacerbations and discontinuations due to adverse events (AE). Networks of evidence were based on treatment- and dose-specific nodes except for budesonide/formoterol for which different devices were combined. Interpretation of results was based on absolute differences/ratios and Bayesian probabilities for treatments to perform better than others (P), where P≤15% indicated a smaller effect and P≥85% a larger effect. Vague prior distributions were used. Selection of fixed versus random effects was based on the Deviance Information Criterion (DIC). **RESULTS:** 6/9/5 studies reported results at 16/26/52 weeks respectively. Analyses indicated that ICS/LABA were associated with higher improvement in FEV1 (D) compared to roflumilast (D: 0.050L to 0.060L, P≥94%), ICS/LABA were comparable to each other and all active treatments performed better compared to placebo. In terms of COPD exacerbations, at 26 weeks, active treatments were overall comparable and performed better than placebo. At 52 weeks, salmeterol/fluticasone propionate had lower COPD exacerbation rates than roflumilast (OR: 0.52, P=94%). ICS/LABA were associated with lower discontinuations due to AE rates compared to roflumilast (OR: 0.10 to 0.30, P≥98%). Among ICS/LABA, mometasone furoate/formoterol 200/10µg had a lower rate of discontinuations compared to salmeterol/fluticasone propionate and fluticasone furoate/vilanterol. **CONCLUSIONS:** This network meta-analysis of treatment in COPD suggested that ICS/LABA were associated with better efficacy and safety compared to roflumilast. However, roflumilast trials mainly focused on Asian patients and more severe populations which may have impacted the treatment effect observed.

PRS9

EVOLUTION OF TIOTROPIUM EFFICACY VS. PLACEBO OVER TIME FOR THE MAINTENANCE THERAPY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE: FROM INVESTIGATIONAL PRODUCT TO ACTIVE REFERENCE

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OBJECTIVES: Previous studies have demonstrated substantial variation of the relative efficacy of widely used drugs over time. Changes in population characteristics or variation in the placebo response may be potential influencers. We used tiotropium as a treatment to examine this phenomenon as it has commonly been used as a reference treatment over time in Chronic Obstructive Pulmonary Disease (COPD). We aimed to assess the evolution of the relative efficacy of inhaled tiotropium against placebo, between launch and the latest assessment. **METHODS:** We performed a systematic literature review of randomized-controlled trials (RCTs) of adults suffering from COPD in Medline from 2000 (launch) to 2012. RCTs evaluating tiotropium 18 µg as a maintenance treatment for COPD were included in the analyses. Efficacy outcomes evaluated included change from baseline in trough forced expiratory volume in 1 second (FEV1) and COPD exacerbations leading to hospitalizations. Efficacy of tiotropium was presented as the mean difference to placebo. **RESULTS:** Difference in change from baseline in FEV1 versus placebo was evaluated in 21 RCTs. The relative effect of tiotropium increased over time, ranging from 0.084 to 0.150 in 2000 (launch) and from 0.120 to 0.189 in 2012. Difference in rates of exacerbations versus placebo was reported in 24 studies. The relative effect of tiotropium was found to decrease over time for this outcome. This trend was partly explained by an increase in placebo effect. **CONCLUSIONS:** We identified variations in the relative efficacy of tiotropium over time on two major outcomes for assessing drug relativeness effectiveness in COPD. Further research is required to understand these changes and the implications for evaluating the relative effectiveness of a new drug versus already marketed ones. Time of marketing authorization may not be the appropriate time to assess the relative effectiveness of a new drug.

PRS10

CAN WE IMPROVE THE INHALATION TECHNIQUES IN PATIENT WITH COPD?. TIEPOC STUDY

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OBJECTIVES: to test the efficacy of two educational interventions to improve the inhalation techniques in patients with Chronic Obstructive Pulmonary Disease. **METHODS:** Design: Multicenter Randomised Controlled Trial ISRCTN60147249. Patients: 220 COPD patients (to detect a difference between groups of 25%, 80% statistical power, 95% confidence level, 40% expected losses), with inhaled treatment, written consent. Non-probabilistic consecutive sampling. Allocation: Patients were randomised using block randomization into three cohorts: InterA, IntervB, control. Variables: Primary outcomes: Performance of correct inhalation technique. Secondary outcomes: Pick flow, Baseline dyspnea index (BDI), Functional status (forced spirometry). Interventions: Intervention-A: Written information. A leaflet with the correct inhalation technique for the main inhaler devices used in our area. Intervention-B: Intervention-A + individual training (by instructors). Follow-up: 12 month, visits: baseline, 1 month, 3rd month, 6th month, 12th month. Statiscal analysis: Mean, frequency, 95% confidence interval at baseline. Number Needed to Treat for a benefit (NNT) was calculated. Intention to treat analysis. **RESULTS:** Predominance of males (85.5%), mean age 70.54 years (CI95%, 69.38-71.7); FEV1(mean)=54.2% (IC95%, 51.81-56.55), mixed respiratory pattern (62.5%). Severity stage: 11.4% mild, 47.4% Moderate, 41.4% Severe. Pharmacological treatment: inhaled-beta2-adrenergic (81.7%); inhaled-anticholinergic (76.3%); inhaled-corticosteroids (75.3%); mucolitycs (13.7%); xanthine (5%); oral-corticosteroids (0.9%). BDI: grade 2. There were no statistically significative differences between groups at baseline. Primary outcome: The 88.1% of patients did not perform a correct inhalation technique: 88.5% with Handihaler, 83.3% with Turbuhaler, 81.7% with Accuhaler and 79.1% with pMDI. There were statistically significative differences between control and intervention A (p=0.023), NNT= 8.62 (IC95%, 4.63-62.5). There were statistically significative differences between intervention B versus control (p<0.0001), 1.74 (IC95%, 1.47-2.17). **CONCLUSIONS:** The knowledge about the correct performance of inhalation techniques is poor in patient with COPD. The performance of a correct inhalation technique improves with monitor training.

PRS11

CLINICAL EVALUATION OF KANAKASAVA AND SWASANANDAM GULIKA IN BRONCHIAL ASTHMA

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OBJECTIVES: To evaluate the clinical effectiveness of Kanakasava and Swasanandam Gulika in Bronchial Asthma. **METHODS:** A randomized single blind clinical study with pretest and posttest design in 2 groups's standard and trail were adopted, where the patients were given treatment with specific duration with follow up. In total 342 patients were selected from the OPD and IPD of Muniyal Institute of Ayurveda Medical Sciences Manipal enrolled for the present study out of which 22 were dropped out from the study. Routine hematological, bio-chemical and urine analysis were recorded. The main Signs and Symptoms Breathlessness, Wheezing, cough, Sneezing, Dysponea, head ache, were taken for assessment as symptoms grade parameters. Peak expiatory flow rate (PEFR), Absolute Eosinophil count (AEC), and ESR also taken for the assessment as Laboratory parameters. Data obtained from the above mentioned study was statistically analyzed by using the Z test. **RESULTS:** Kanakasava and Swasanandam Gulika provided 67.5%. relief in Wheezing, 75.86% relief in Dysponea , 66.07%, relief in cough, 54.78% relief in Sneezing and 43.22% relief in Head ache which were statistically highly significant result p<0.001, where as in PEFR, AEC and ESR provided 92.85%, 23% and 35.89% relief respectively which were also statistically highly significant result p<0.001. **CONCLUSIONS:** Kanakasava and Swasanandam Gulika appear to be beneficial in Bronchial Asthma along with its symptoms. Bronchial Asthma is considered as chronic airway inflammatory disease. The effects in every condition and in complications are still being evaluated.

PRS12

USE OF XANTHINES IN THE TREATMENT OF CHRONIC RESPIRATORY DISEASES IN SERBIA, COMPARED WITH THE SCANDINAVIAN COUNTRIES FROM 2004 TO 2013

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OBJECTIVES: Respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD), cause about 1 million deaths annually in the WHO European Region. Xanthines (e.g. theophylline, aminophylline) are recommended for treating severe exacerbations of COPD, when short-acting bronchodilators do not produce